

GCCAGGTCTGGCACCATGCACTAGGATACCCAGAACGCTGCAAGGCCACGCC
CTCCTCACTTCAGGGGTCACTCTCCCCATTGCCACCACCCACCATGGCTGGG
GATCGGCTCCCGAGGAAGGTGATGGACGCAAAGAACTGGCCAGCCTGCTGC
GTGGCGGGCCTGGGGGACCCCTGGTTCATCGACAGCCGGTCCTTCGTGGAGTAT
AACAGCTGCCACGTGCTGAGCTCTGTGAATATCTGCTGTTCAAAGCTGGTGAA
GCGGCGCCTTCAGCAGGGGAAAAGTGACAATTGCTGAGCTTATCCAGCCTGCTA
CACGGAGCCAGGTGGATGCCACAGAACACAGGATGTAGTGGTGTATGACCA
GAGCACACGAGATGCCAGCGTGCTGGCAGCAGACAGCTTCCTGTCCATCCTGC
TCAGCAAGCTGGACGGCTGCTTCGACAGTGTGGCCATCCTCACAGGAGGCTTC
GCCACCTTCTCCTCCTGCTTCCCTGGCCTCTGTGAGGGCAAGCCTGCCACTCTA
CCGTCCATGAGCCTCTCTCAGCCCTGCCTGCCTGTGCCCAGTGTGCGCCTGACC
CGAATCCTGCCTCACCTCTACCTGGGCTCTCAGAAAGATGTCTTGAACAAGGA
TCTGATGACCCAAAACGGAATAAGCTATGTCCTCAATGCCAGCAACTCCTGCC
CTAAACCGGACTTCATCTGTGAGAGCCGTTTCATGCGTATCCCCATCAATGAC
AACTACTGTGAAAAGCTGCTGCCCTGGCTGGACAAGTCCATCGAGTTTATTGA
TAAAGCCAAGCTGTCCAGCTGCCAAGTCATTGTTCACTGTCTGGCTGGCATCTC
TCGCTCTGCCACCATTGCCATCGCGTACATCATGAAAACCATGGGCATGTCTTC
TGACGACGCATACAGGTTTGTGAAGGATCGGCGCCCCTCCATCTCGCCCAACT
TCAACTTCCTGGGCCAGTTGCTGGAGTATGAGAGGAGTCTGAAGCTGCTGGCT
GCCCTGCAGACTGATGGACCTCACTTGGGGACCCCTGAGCCCTCATGGGCCC
GGCAGCAGGCATCCCACTGCCCCGGCTGCCACCATCTACCTCAGAGAGCGCTG
CCACTGGGAGCGAGGCAGCCACCGCAGCCAGGGAGGGCAGCCCAAGTGCTGG
AGGGGATGCTCCGATCCCCAGCACAGCTCCAGCCACCAGCGCGCTGCAGCAG
GGCCTGCGTGGCCTGCACCTCTCCTCTGACCGCCTCCAGGACACCAACCGCCT
CAAGCGTTCCTTTTCCCTGGACATCAAGTCGGCCTATGCACCCAGCAGGAGGC
CCGACTTTCCCGGCCACCCGACCCCGGTGAAGCCCCGAAGCTCTGCAAGCTG
GACAGCCCGTCTGGGGGCACACTGGGCCTGCCCTCGCCAGCCAGACAGCCC
GGACTCCGTTCCAGAGTGCCGCCCACGACCCCGCCGGCGACGCCCCCGGCTA
GTTTCGCTGCCCCGCTCCCCCGCGCATGGTCTGGGCCTGAACTTTGGAGACACG
GCCCCGAGACTCCACGGCACGGCCTCTCGGCCCTGTGCGCGCCCGGGCTGCC
TGGCCCTGGCCAGCCGGCTGGCCCCGGGGGCTGGGTGCCGCCACTGGACTCCC
CAGGCACACCGTCGCCCCGACGGCCCCCTGGTGCTTCAGCCCCGAGGGCGCGCA
GGGTCCAGGCGCTGTGTTCTCCGCCTTTGGCCGGGTAAGTGCAGGCGCACCTG
GACCCGGTAACAGCAGCAGCAGCGGTGGTGGTGGTGGTGGTGGTGGCGGCGG
CGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGG
CAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAG
CGGAGGCGGGATGTGCGGACCGGCTGGCCCGAGGAGCCTGCTGCAGATGCAC
AGTTCAAGAGGCGCAGCTGCCAGATGGAGTTCGAAGAGGGCATGGTGGAGGG
GCGGGCACGTGGCGAGGAGCTGGCAGCCCTGGGCAAGCAAACCAGCTTCTCT
GGCAGCGTGGAGGTCATCGAAGTATCGTGACCCTTCAGAAGTCCCTGTGCCCT
TGCTCCAGCCAGGCCAGGTATAAATATATATTATATATAAAACACACAGAAAA
GGTAAATGGTTTTACTGCAATTTTTATCAAGAAGTAAATATTTTCGATTTTTAT
TTATTTAAGCTAGTGATCTGGCAACTGTGCGGGGCGGCCCTAAAGCTCTGTTTT
TACTGTCTGGTATTTAACTGAAACAGGTTTCTAAGCAATATGAGGCCACCTT
CAATCCCAAAGTGGGTTGACAGGCCTGGGCCCCCTCCTTGCCCCCTCCCCCTCTGG
AAACATTACTGACCTTTCAAAGAGCTGCCAGCTTTCCTGCACTTTTTACATAA
GAAAAAAGGGGGGGGGGGGAA (SEQ ID NO:1)

FIGURE 1

underlined = deleted in targeting construct

[] = sequence flanking Neo insert in targeting construct

[GCCAGGTCTGGCACCATTGCACTAGGATACCCAGAACGCTGCAAGGCCACGCCCTCCTCAC
TTCAGGGGTCACCTCTCCCCATTGCCCACCACCCACCATTGGCTGGGGATCGGCTCCCGAG
GAAGGTGATGGACGCAAAGAAA] CTGGCCAGCCTGCTGCGTGGCGGGCCTGGGGGACCCTT
GGTCATCGACAGCCGGTCCTTCGTGGAGTATAACAGCTGCCACGTGCTGAGCTCTGTGAA
TATCTGCTGTTCAAAGCTGGTGAAGCGGCGCCTTCAGCAGGGAAAAGTGACAATTGCTGA
GCTT [ATCCAGCCTGCTACACGGAGCCAG] GTGGATGCCACAGAACCACAGGATGTAGTGGT
GTATGACCAGAGCACACGAGATGCCAGCGTGCTGGCAGCAGACAGCTTCCTGTCCATCCT
GCTCAGCAAGCTGGACGGCTGCTTCGACAGTGTGGCCATCCTCACAGGAGGCTTCGCCAC
CTTCTCCTCCTGCTTCCCTGGCCTCTGTGAGGGCAAGCCTGCCACTCTACCGTCCATGAG
CCTCTCTCAGCCCTGCCTGCCTGTGCCAGTGTGGCCTGACCCGAATCCTGCCTCACCT
CTACCTGGGCTCTCAGAAAGATGTCTTGAACAAGGATCTGATGACCCAAAACGGAATAAG
CTATGTCTCAATGCCAGCAACTCCTGCCCTAAACCGGACTTCATCTGTGAGAGCCGTTT
CATGCGTATCCCCATCAATGACAACTACTGTGAAAAGCTGCTGCCCTGGCTGGACAAGTC
CATCGAGTTTATTGATAAAGCCAAGCTGTCCAGCTGCCAAGTCATTGTTCACTGTCTGGC
TGGCATCTCTCGCTCTGCCACCATTGCCATCGCGTACATCATGAAAACCATGGGCATGTC
TTCTGACGACGCATACAGGTTTGTGAAGGATCGGCGCCCCCTCCATCTCGCCCAACTTCAA
CTTCCTGGGCCAGTTGCTGGAGTATGAGAGGAGTCTGAAGCTGCTGGCTGCCCTGCAGAC
TGATGGACCTCACTTGGGGACCCCTGAGCCCTCATGGGCCCCGGCAGCAGGCATCCCACT
GCCCCGGCTGCCACCATCTACCTCAGAGAGCGCTGCCACTGGGAGCGAGGCAGCCACCGC
AGCCAGGGAGGGCAGCCCAAGTGCTGGAGGGGATGCTCCGATCCCCAGCACAGCTCCAGC
CACCAGCGCGCTGCAGCAGGGCCTGCGTGGCCTGCACCTCTCCTCTGACCGCCTCCAGGA
CACCAACCGCCTCAAGCGTTCTTTTCCCTGGACATCAAGTCGGCCTATGCACCCAGCAG
GAGGCCCCGACTTTCCCGGGCCACCCGACCCCGGTGAAGCCCCGAAGCTCTGCAAGCTGGA
CAGCCCGTCTGGGGGCACACTGGGCCTGCCCTCGCCCAGCCCAGACAGCCCGGACTCCGT
TCCAGAGTGCCGCCCACGACCCCGCCGGCGACGCCCCCGGCTAGTTGCGCTGCCCGCTC
CCCCGCGCATGGTCTGGGCCTGAACTTTGGAGACACGGCCCGGCGAGCTCCACGGCACGG
CCTCTCGGCCCTGTCGGCGCCCCGGGCTGCCTGGCCCTGGCCAGCCGGCTGGCCCCGGGGG
CTGGGTGCCGCCACTGGACTCCCCAGGCACACCGTCGCCCCGACGGCCCTGGTGCTTCAG
CCCCGAGGGCGCGCAGGGTCCAGGCGCTGTGTTCTCCGCCTTTGGCCGGGTAAGTGCAGG
CGCACCTGGACCCGGTAACAGCAGCAGCAGCGGTGGTGGTGGTGGTGGTGGTGGCGGCGG
CGG
CAGCAGCAGCAGCAGCAGCAGTAGTAGTAGTAGTAGTAGTACCTGCGGAGGCGGGATGTGCG
GACCGGCTGGCCCCGAGGAGCCTGCTGCAGATGCACAGTTCAAGAGGCGCAGCTGCCAGAT
GGAGTTCTGAAGAGGGCATGGTGGAGGGGCGGGCACGTGGCGAGGAGCTGGCAGCCCTGGG
CAAGCAAACCAGCTTCTCTGGCAGCGTGGAGGTCATCGAAGTATCGTGACCCCTTCAGAAG
TCCCTGTGCCCTTGCTCCAGCCAGGCCAGGTATAAATATATATTATATATAAAACACACA
GAAAAGGTAAATGGTTTTACTGCAATTTTTATCAAGAAGTAAATATTTTCGATTTTTTATT
TATTTAAGCTAGTGATCTGGCAACTGTGCGGGGCGGCCCTAAAGCTCTGTTTTTACTGTC
TGGTATTTAACTGAAACAGGTTTCTAAGCAATATGAGGCCACCTTCAATCCCAAACCTGG
GTTGACAGGCCTGGGCCCCCTCCTTGCCCCCTCCCTCTGGAAACATTACTGACCTTTCAA
GAGCTGCCCAGCTTTCCTGCACTTTTTTACATAAGAAAAAAGGGGGGGGGGAA

FIGURE 2A

Gene Sequence Structure *

143 bp

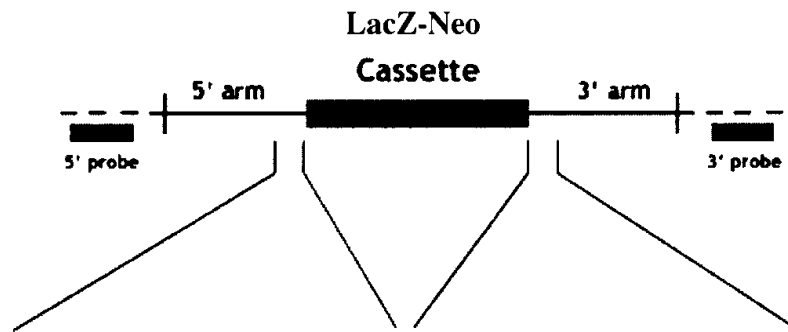
Sequence Deleted

304 bp

Size of full-length
cDNA: 2453 bp

Targeting Vector* (genomic sequence)

Arm Length:
5': 2.5 kb
3': 2 kb



———— Targeting Vector
- - - - Endogenous Locus

* Not drawn to scale

5' > TCCTGGGAGCCAGCTATAGCT
ACCCAGATCCCACCATCTGCTGAC
TATTCACCTTTCCCCAGGTCTGG
CACCATGCACTAGGATACCCAGAA
CGCTGCAAGGCCACGCCCTCCTCA
CTTCAGGGGTCACCTCTCCCATG
CCCACCACCCACCATGGCTGGGG
ATCGGCTCCCGAGGAAGGTGATGG
ACGCAAAGAAA<3'
(SEQ ID NO:2)

5' > ATCCAGCCTGCTACACGAAGC
CAGGTACCTGTGGCCCACCCTTGC
ATGCGTCTTCAGGGCTGACCATTG
CTGAGCAAACAGACCTATGTCACC
TCTGAAAGAGACAGAGGAGCTCCC
AGGCCTGGTGCCAAGAGTCCTCTG
ATAAGGCATTTCCTCCGCTGTC
CCTCCGTTCCAAACAGGGTTCCTT
GGGGTCAGAGC<3'
(SEQ ID NO:3)

FIGURE 2B